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09/350,401	07/08/1999	ALESSANDRO SETTE	2473.0060008/paj/m-m	8008

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EXAMINER

SCHWADRON, RONALD B

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1644

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06/27/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/350,401	Applicant(s) SETTE ET AL.
	Examiner Ron Schwadron, Ph.D.	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 63-77 is/are pending in the application.
 4a) Of the above claim(s) 65,68,70,71 and 75-77 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 63,64,66,67,69,72-74 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/30/10</u> . | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) <input type="checkbox"/> Notice of Informal Patent Application
6) <input type="checkbox"/> Other: _____. |
|--|--|

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/20/10 has been entered.

2. Claims 63,64,66,67,69,72-74 are under consideration. Claims 75-77 depend from withdrawn claim 70 and are therefore withdrawn from consideration.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 72-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 72-74 lack antecedent basis in claim 63 because the "immunogenic composition" recited in said claims lacks antecedent basis in claim 63 which is drawn to a peptide.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 64,66,67,69,72-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

1) There is no support in the specification as originally filed for the composition of claim 64/67. The specification discloses vaccines or pharmaceutical compositions containing *a pharmaceutically acceptable carrier*, but does not disclose the scope of claim 64 which is a composition other than vaccine or pharmaceutical containing pharmaceutically acceptable carriers.

Regarding applicants comments, the cited passages of the specification are not drawn to immunogenic compositions containing *a pharmaceutically acceptable carrier*. Regarding applicants comments about the specification, page 41, said passage refers to a vaccine composition. Regarding applicants comments about original claims 4-8, said claims are drawn to pharmaceutical compositions. The specification discloses vaccines or pharmaceutical compositions containing *a pharmaceutically acceptable carrier*, but does not disclose the scope of claim 64 which is a composition other than vaccine or pharmaceutical containing pharmaceutically acceptable carriers. The composition of claim 1 does not have a pharmaceutically acceptable carrier wherein the only such compositions containing a pharmaceutically acceptable carrier are the aforementioned pharmaceutical compositions. The cited passages of the specification are limited to a disclosure of pharmaceutical or vaccine compositions. Regarding the various in vitro assays to which applicant refers, none of said assays are drawn to compositions containing *a pharmaceutically acceptable carrier* for administration in vivo to humans. Regarding applicants comments about Wang et al. and FIA, said example is limited to administration of said composition to mice, not humans and is also limited to use of FIA. The cited passages of the specification, page 9 and 43 refers to vaccine compositions. Regarding applicants comments about page 41, said passage refers to vaccine compositions, with no definition of said term that would contradict the art known meaning of said term.

2) There is no support in the specification as originally filed for the recitation of “wherein said one or more second peptides is a cytotoxic T cell (CTL)- inducing peptide or a helper T cell (HTL)-inducing peptide” in claim 66/69. Regarding applicants comments, the aforementioned composition is not disclosed in the cited pages of the specification. There is no support in the specification as originally filed for the scope of the claimed inventions (e.g. the claimed inventions constitutes new matter).

Regarding applicants comments, whilst the cited passages disclose vaccine compositions containing the components under consideration, the instant claims encompass nonvaccine compositions containing the aforementioned ingredients that are not disclosed in the specification. Regarding the cited passages of the specification, pages 18 and 41, said passages are not drawn to the particular composition recited in the instant claims. The example on page 84 is drawn to a vaccine composition which is not the composition under consideration in the instant claims.

3) There is no support in the specification as originally filed for the composition of claims 69. The specification discloses the peptide of claim 69 linked to a CTL epitope or contained in a vaccine composition, but does not disclose the claimed composition which is not a vaccine and wherein the peptides are not linked.

Regarding applicants comments, whilst the cited passages disclose vaccine compositions containing the components under consideration, the instant claims encompass nonvaccine compositions containing the aforementioned ingredients that are not disclosed in the specification. In addition, regarding the cited passage of page 84 of the specification, said passage refers to "epitopes from the various disease associated sources" wherein the HTL peptides recited in the instant claims are not disease associated HTL. Regarding applicants comments, the quoted passage of the specification from page 5 of the instant amendment states: "A polyepitopic peptide composition ... **for the administration to individuals at risk for both HBV and HCV infection**". Thus, the composition referred to in said passage is a vaccine. Regarding the cited passage of page 50, said passage comes from section IV.K.2 which is a subsection of section IV.K (aka Vaccine Compositions).

7. Claims 64,67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the claimed immunogenic composition containing a pharmaceutically acceptable carrier. The specification does not disclose how to use the instant invention for the in vivo treatment/prevention of HBV in humans. Applicant has

not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the instant invention disclosed in the specification is the in vivo treatment/prevention of HBV infection in humans. The state of the art is such that is unpredictable in the absence of appropriate evidence as to how the instant invention could be used for the in vivo treatment/prevention of HBV infection in humans.

Judge Lourie stated in Enzo Biochem Inc. v. Calgene Inc. CAFC 52 USPQ2d 1129 that:

The statutory basis for the enablement requirement is found in Section 112, Para. 1, which provides in relevant part that:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the same. . . .35 U.S.C. Section 112, Para. 1 (1994). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " Genentech, Inc. v. Novo Nordisk, A/S , 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright , 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see Hybritech, Inc. v. Monoclonal Antibodies, Inc. , 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), which in this case is October 20, 1983 for both the '931 and '149 patents.

We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g., Wands , 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In In re Wands , we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

Regarding *Wands* factors 4,5,7,8, the claimed inventions are drawn to a immunogenic composition containing a pharmaceutically acceptable carrier wherein *the only use for compositions containing a pharmaceutically acceptable carrier disclosed in the specification is to treat/prevent HBV infection*. The substantial/real life use for the claimed inventions are preventing and treating HBV infection in humans. There is currently no known pharmaceutical composition containing a single HBV peptide for treating or preventing HBV in humans. Basalp et al. teach that the currently used HBV vaccine contains intact HBV surface antigen (HBs, see column 1, page 2).

The claimed invention does not contain intact HBs and only contains a single peptide derived from HBV polymerase. There is no evidence of record that intact polymerase (or the pol derived peptide recited in the claim) can be used to treat HBV infection in humans. Basalp et al. teach that antibody responses against HBs that are produced by the HBV vaccine are an important component of the mechanism of action of the HBV vaccine (see page 1, column 1, continued on page 2 and pages 4-6). There is no evidence of record that the peptide recited in the claim can elicit a protective antibody response for the treatment of HBV infection. In addition, the peptide recited in the claims does not bind most HLA alleles and therefore would not even elicit CTL in most individuals.

Thus, the state of the art is that it is highly unpredictable whether the peptide recited in the claims could be used as in a composition to treat/prevent HBV infection in humans. As per *Wands* factor (8), the claimed inventions are used for preventing and treating HBV infection. Regarding *Wands* factors 1-3,7 there is no disclosure in the specification of experimental data indicating that the claimed peptide can be used to prevent or treat

HBV in vivo in humans. Thus, use of a particular peptide for treatment/prevention of HBV infection is an unpredictable field where extensive experimentation and guidance would be required to use the claimed vaccine or pharmaceutical composition in vivo in humans. The specification provides no evidence predictive of whether the claimed invention could be used in vivo in humans to treat/prevent malarial infection. Regarding Wands factor 6, the relative skill of those in the art is high (e.g. Ph.D. or M.D.). Undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. See In re Wands 8 USPQ2d 1400(CAFC 1988).

Regarding applicants comments, the claimed invention is drawn to a composition *wherein the intended use for said composition disclosed in the specification is the in vivo treatment of disease in humans*. Regarding applicants comments about other uses, as per the new matter rejection addressed above, the only compositions disclosed in the specification with a pharmaceutically acceptable carrier are pharmaceutical/vaccine compositions for treatment of disease. The claimed inventions are drawn to a composition that can be used to treat/prevent HBV infection. The substantial/real life use for the claimed inventions are preventing and treating HBV infection in humans. There is currently no known composition containing a single HBV peptide for treating or preventing HBV in humans. Basalp et al. teach that the currently used HBV vaccine contains intact HBV surface antigen (HBs, see column 1, page 2). The claimed invention does not contain intact HBs and only contains a single peptide derived from HBV polymerase. There is no evidence of record that intact polymerase (or the pol derived peptide recited in the claim) can be used to treat HBV infection in humans. Basalp et al. teach that antibody responses against HBs that are produced by the HBV vaccine are an important component of the mechanism of action of the HBV vaccine (see page 1, column 1, continued on page 2 and pages 4-6). There is no evidence of record that the peptide recited in the claim can elicit a protective antibody response for the treatment of HBV infection. In addition, the peptide recited in the claims does not bind most HLA alleles and therefore would not even elicit CTL in most individuals. Thus, the state of the art is that it is highly unpredictable whether the peptide recited in the claims could be used as a pharmaceutical composition to treat/prevent HBV infection in humans. As per Wands factor (8), the claimed inventions are used for preventing and

treating HBV infection. Regarding Wands factors 1-3,7 there is no disclosure in the specification of experimental data indicating that the claimed peptide can be used to prevent or treat HBV in vivo in humans. Thus, use of a particular peptide for treatment/prevention of HBV infection is an unpredictable field where extensive experimentation and guidance would be required to use the claimed vaccine or pharmaceutical composition in vivo in humans. The specification provides no evidence predictive of whether the claimed invention could be used in vivo in humans to treat/prevent HBV infection. Regarding applicants comments, the claims encompass a composition that only contains the particular peptide recited in the claims. Regarding applicants comments about Mizukoshi et al., said reference does not disclose use of the claimed inventions to treat or prevent HBV infection. In fact, said reference does not disclose the administration of any peptide to a patient. The reference refers to immune responses that are found in HBV patients against a plethora of different peptides. The reference does not teach that immunization with any one particular peptide can be used to treat/prevent HBV infection.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. The rejection of claims 63,64,66,67 under 35 U.S.C. 102(e) as being anticipated by Seeger et al. (US Patent 5,360,714) as evidenced by Pasek et al. for the reasons elaborated in the previous Office Action is withdrawn in view of the amended claims and applicants arguments.

10. The peptide of SEQ. ID. NO:638 is free of the prior art.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 63,64,66,67,72-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chisari et al. (US Patent 5,840,303) in view of Guo et al. and Pasek et al.

Chisari et al. teach MHC class I binding peptides derived from HBV polymerase (see abstract and Example VII). Chisari et al. teach compositions containing said peptides and a pharmaceutically acceptable carrier (see column 15, penultimate paragraph). The peptides/compositions can contain a HTL epitope/peptide (see column 12, penultimate paragraph and next paragraph). Chisari et al. teach that it is desirable to identify other MHC class I binding HBV peptides which bind MHC class I alleles other than the specific examples disclosed in said patent (see column 10, last paragraph). The amino acid sequence of HBV pol was known in the art (see Pasek et al., Figure 2). Chisari et al. do not teach that the peptide is SEQ. ID. No:620. Guo et al. teach that CTL recognize viral peptides complexed with MHC (see page 364, first column, last sentence continued on next page). Guo et al. teach that said peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K or R at the c-terminal position (see page 366, second column) and means for determining the identity of such peptides based on a known protein sequence. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Chisari et al. teach MHC class I binding peptides derived from HBV polymerase and that it is desirable to identify MHC class I binding HBV peptides which bind MHC class I alleles other than the specific examples disclosed in said patent, whilst Guo et al. teach that CTL recognize viral peptides complexed with MHC and that peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position and means for determining the

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identity of such peptides based on a known protein sequence. . One of ordinary skill in the art would have been motivated to create the claimed peptide to screen for HBV peptides which were recognized by CTL because Chisari et al. teach that it is desirable to identify CTL epitopes found in HBV and Guo et al. teach that CTL recognize viral peptides complexed with MHC and that peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K/R at the c-terminal position.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is (571)272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/

Primary Examiner, Art Unit 1644

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Primary Examiner, Art Unit 1644